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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,225	10/31/2003	Dan-Hui Dorothy Yang	10021166-1	1504

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AGILENT TECHNOLOGIES, INC.

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EXAMINER

LUM, LEON YUN BON

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/698,225

Applicant(s)

YANG ET AL.

Examiner

Leon Y Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1 and 11 recite that "R² is a chemically inert hydrophilic moiety" (line 7 of the claims). However, the specification does not provide support for a chemically inert R² group. The specification recites on page 16, line 10, that "R² is -(OCH₂CH₂)_k-H" and also recites on page 20, lines 6-8, the compound "undecenyltrichlorosilane (UTS)", wherein the terminal olefinic moiety of UTS is converted to a hydroxyl group. Both a hydroxyl group and -(OCH₂CH₂)_k-H are functional groups that produce covalent bonding and are not considered to provide non-covalent bonding, as is known to one of ordinary skill in the art. Since there is no other example of R² recited in the specification, the phrase "R² is a chemically inert hydrophilic moiety" in the instant claims is not supported by the specification.

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3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are as follows: The claim recites "low background signal" in line 2 of the claim. However, it is unclear as to how the signal is obtained and how it relates to the binding of target protein by probe proteins. Do the blocking proteins provide the signal themselves and do the target proteins also provide a signal for comparison purposes? Applicant is invited to clarify the claim.

6. Claim 18 is drawn to R^2 selected from hydroxyl, acetyl, carboxyl, amino, amide, methoxy, ethoxyl, propoxyl, and $-(OCH_2CH_2)_k-H$, wherein R^2 is a chemically inert hydrophilic moiety, as recited in line 7 of the parent claim, claim 1. However, the limitations of hydroxyl, acetyl, carboxyl and amino are well-known reactive groups, and it is unclear as to how the groups can be reactive and chemically inert at the same time. The definition of chemically inert on page 7, lines 23-31, of the specification disclose that groups referred to as chemically inert will not react to form a covalent bond. However, one of ordinary skill in the art would recognize that the hydroxyl, acetyl,

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carboxyl and amino groups do form covalent bonds. The groups are therefore being claimed in a manner that is contradictory to their definition in the specification.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-8, 10-13, and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haab et al (Genome Biology 2001, 2(2)) in view of Lefkowitz et al (US 6,258,454 B1) and in light of Kusnezow et al (Journal of Molecular Recognition, 2003, 16).

Haab et al reference teaches a protein bioarray and method providing a substrate comprising a solid support and a surface modification layer bound to the solid support, providing at least two solutions, each solution comprising a probe protein, and depositing the solutions onto discrete sites on the substrate, each solution being deposited onto its own discrete site, wherein each probe protein becomes non-covalently attached to the substrate at its respective discrete site, by disclosing a method wherein microarrays were constructed by printing microscopic spots of either antibodies or antigens onto a modified glass surface, wherein the microarrays contained six to twelve spots of each antibody or antigen, wherein one array contained 114 different antibodies and another array contained 116 different antigens, wherein the antibody and antigen spots are discrete and isolated from other spots by 375 μm spacing (page 2, right column, 1st full paragraph, lines 4-8; and Figures 1-2 and captions), and wherein the modified glass surface is a poly-L-lysine coated microscope slide (page 12, left column, last paragraph, lines 1-19). Although Haab et al reference does not specifically teach that the antibodies or antigen non-covalently bind to the

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microscope slides, it is well known in the art that antibody binding to poly-L-lysine layers occurs through non-covalent bonds, as disclosed by Kusnezow et al (Table 1).

However, Haab et al reference fails to teach the surface modification layer comprising at least a first moiety having the structure $-\text{Si}-\text{R}^1$ and a second moiety having the structure $-\text{Si}-\text{L}-\text{R}^2$, wherein R^1 is a chemically inert moiety selected from the group consisting of C_3 to C_{30} alkyl and benzyl optionally substituted with 1 to 5 halogen atoms, L is a linking group, and R^2 is a chemically inert hydrophilic moiety.

Lefkowitz et al reference discloses the step of derivatizing a glass substrate with two compositions, n-decyltrichlorosilane (NTS) and undecenyltrichlorosilane (UTS) to produce two silanes, $-\text{Si}-\text{R}^1$, and $-\text{Si}-(\text{L})_n-\text{R}^2$, wherein n is 1, wherein R^1 is chemically inert, and wherein R^1 is an alkyl group in the range of 2 to 24 carbon atoms, and may be benzyl, either unsubstituted or substituted with 1 to 5 halogen atoms, wherein L is a linker, and wherein R^2 comprises either a functional group or a modifiable group that can be converted into a functional group (column 6, line 59 to column 7, line 58; and column 9, lines 45-51), in order to reduce surface energy and constrain droplets of liquid that are applied to a substrate surface (column 2, lines 17-22), wherein the silanes are derivatized on glass (column 6, lines 38-55, especially line 55) and can bind to the L-form of lysine (column 5, lines 32-36).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Haab et al with step of derivatizing a glass substrate with two compositions, n-decyltrichlorosilane (NTS) and undecenyltrichlorosilane (UTS) to produce two silanes, $-\text{Si}-\text{R}^1$, and $-\text{Si}-(\text{L})_n-\text{R}^2$, wherein n is 1, wherein R^1 is chemically

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inert, and wherein R^1 is an alkyl group in the range of 2 to 24 carbon atoms, and may be benzyl, either unsubstituted or substituted with 1 to 5 halogen, wherein L is a linker, and wherein R^2 comprises either a functional group or a modifiable group that can be converted into a functional group, as taught by Lefkowitz et al, in order to reduce surface energy and constrain droplets of liquid that are applied to a substrate surface. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in using two silanes, $-\text{Si}-R^1$, and $-\text{Si}-(\text{L})_n-R^2$, as surface modification layers, as taught by Lefkowitz et al, in the method of Haab et al, since Haab et al teach modification of glass surfaces such as microscope slides and the non-covalent binding of antibodies to a poly-L-lysine layer, and the two silanes taught by Lefkowitz et al are also derivatized on glass surfaces and have the ability to bind to the L-form of lysine.

With regards to claim 2, Haab et al teach the step further comprising drying the substrate after depositing the solutions, by disclosing that the coated slides were spun dry and further dried for 1 h at 80°C in a vacuum oven (page 12, left column, last paragraph, lines 13-19).

With regards to claims 3-6 and 12-13, Haab et al teach the step further comprising contacting the substrate with a blocking composition comprising a blocking protein, wherein the blocking protein becomes non-covalently attached to the substrate, wherein the discrete sites are separated by intervening areas, and the blocking protein becomes non-covalently attached to the substrate at the intervening areas and at the discrete sites, wherein the blocking composition comprises a plurality of blocking

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proteins, and wherein the plurality of blocking proteins are selected to provide low background signal relative to binding of target protein by the probe proteins, by disclosing an antibody array with spotted antibodies separated by regions on the slides not coated with antibodies, as stated above (Figures 1-2), and by disclosing the steps wherein the arrays were transferred to a 3% non-fat milk/PBS/0.02% sodium azide blocking solution (page 12 right column, 1st paragraph, lines 5-7), and wherein FCS is added to solution mixes in order to decrease background signal from non-specific adsorption of labeled protein (page 8, left column, last paragraph, lines 1-10). By transferring the slide to a blocking solution, the entire slide, including intervening areas, are subjected to non-covalent binding by proteins in the blocking solution. In addition, it is well known in the art that milk contains a plurality of proteins and the 3% non-fat milk/PBS/0.02% sodium azide blocking solution would comprise a blocking solution with a plurality of blocking proteins.

With regards to claims 7-8, 10, and 15, Haab et al teach the step wherein at least one solution comprises a probe protein that is different from at least one other probe protein in another solution, the step, wherein least fifty solutions are provided, the step of depositing the solutions comprises using an inkjet apparatus to deliver one or more droplets of each solution to its respective discrete site, and that the solid support comprises glass, by disclosing the step wherein microarrays were constructed by printing microscopic spots of either antibodies or antigens onto a modified glass surface, wherein the microarrays contained six to twelve spots of each antibody or antigen, wherein one array contained 114 different antibodies and another array

contained 116 different antigens, as stated above (page 2, right column, 1st full paragraph, lines 4-8; and Figures 1-2 and captions).

With regards to claims 16-17, Lefkowitz et al teach that the second moiety comprises from about 0.5% to about 30% of the modification layer, by disclosing that the second silane, UTS, is 2.5 wt.% (column 9, lines 45-50).

With regards to claim 18, Lefkowitz et al teach that R² is hydroxyl, by disclosing that R² may be a functional group such as hydroxyl, as stated above (column 7, lines 49-50).

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haab et al (Genome Biology 2(2), 2001) in view of Lefkowitz et al (US 6,258,454 B1) and in light of Kusnezow et al (Journal of Molecular Recognition 16, 2003) as applied to claim 1 above, and further in view of BD Biosciences (Clontech, April 2002).

Haab et al and Lefkowitz et al references have been disclosed above, but fail to teach that least 250 solutions are provided.

BD Biosciences reference teaches providing a microarray of 378 monoclonal antibodies, in order to assay hundreds of proteins on a single platform simultaneously (1st page, left column, 1st full paragraph; and Figure 1 and captions).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of claim 1 with the step of providing a microarray of 378 monoclonal antibodies, as taught by BD Biosciences, in order to assay hundreds of proteins on a single platform simultaneously. One of ordinary skill in the art at the time

of the invention would have reasonable expectation of success in providing 378 monoclonal antibodies, as taught by BD Biosciences, in the method of Haab et al and Lefkowitz et al, since Haab et al and Lefkowitz et al teach arrays of antibodies on solid supports, and the monoclonal antibodies taught by BD Biosciences are examples of antibodies that can also be immobilized to a solid support.

In addition, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the invention of Haab et al and Lefkowitz et al, by spotting a glass slide with 250 separate antibodies, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

12. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haab et al (Genome Biology 2(2), 2001) in view of Lefkowitz et al (US 6,258,454 B1) and in light of Kusnezow et al (Journal of Molecular Recognition 16, 2003) as applied to claim 1 above, and further in view of Silzel et al (Clinical Chemistry, 1998, 44(9)).

Haab et al and Lefkowitz et al references have been disclosed above, but fail to teach that each discrete site is in the range from 30 to 150 micrometers in diameter.

Silzel et al reference discloses jet-printed spots of antibody reagent having diameters of 100 μm , in order to reduce the size of binding assays for reduced costs, faster chemistry, and equivalent or improved sensitivity (page 2036, left column, entire 2nd paragraph; and page 2043, left column, last paragraph, lines 1-3).

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It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Haab et al and Lefkowitz et al, with the step of providing jet-printed spots of antibody reagent having diameters of 100 μm , as taught by Silzel et al, in order to reduce the size of binding assays for reduced costs, faster chemistry, and equivalent or improved sensitivity. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in applying antibody spots of 100 μm , as taught by Silzel et al, in the method of Haab et al and Lefkowitz et al, since Haab et al and Lefkowitz et al teach printed spots of antibodies and Silzel et al also teaches printed spots of antibodies.

In addition, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the invention of Haab et al and Lefkowitz et al, by creating the probe spots in the range from 30 to 150 micrometers in diameter, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Conclusion

13. No claims are allowed.

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14. The prior art made of record and not relied upon is considered pertinent to

Applicant's disclosure:

Baldeschwieler et al (US 5,847,105) teach surface modification of microscope slides using silane groups.

Fulcrand et al (US 6,319,674 B1) arrays of biomolecules with surface modification using silanes.

Yang et al (US 6,326,083) teach silylation of solid surfaces with a mixture of silylation reagents.

Lefkowitz et al (US 6,444,268 B2) teach silane groups to functionalize surfaces and reduce surface energy.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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